Pflugers Arch - Eur J Physiol (2017) 469:845–846
DOI 10.1007/s00424-017-1973-3

ERRATUM

Erratum to: Sensitisation of TRPV4 by PAR_2 is independent of intracellular calcium signalling and can be mediated by the biased agonist neutrophil elastase

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Published online: 7 April 2017
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Erratum to: Pflugers Arch - Eur J Physiol DOI 10.1007/s00424–014–1539-6

In the context of a follow up study we had difficulties in reproducing some of the findings reported in this study and noticed relevant errors and shortcomings in our experimental procedures and data analysis. We would like to bring these issues and their implications to the attention of our readers to avoid potential pitfalls for future studies trying to build on our work.

The major experimental problem is the following: The statement made in our manuscript (page 690, last sentence of first paragraph) that GSK1016790A was applied in a concentration of 50 nM for 45 s in all subsequent experiments was incorrect. As highlighted in Fig. 1, the TRPV4 currents elicited by GSK1016790A depended on the concentration of the drug and its time of application. Therefore, it is critically important to use the same GSK1016790A concentrations and application times, when comparing GSK1016790A activated TRPV4 currents from different experimental groups. This is why we decided to use a 45 s application time and 50 nM GSK1016790A as standard protocol to estimate TRPV4 currents. However, a detailed re-analysis of the digital raw data from the experiments shown in Figs. 4 to 9 revealed that application times erroneously were quite variable ranging from about 10 s to 60 s. Moreover, we realized that on average application times were relatively short in experimental groups with low TRPV4 currents and long in experimental groups with high TRPV4 currents. In the light of this bias we have to conclude that the different TRPV4 currents observed in the various experimental groups in Figs. 4 to 9 were most likely due to differences in GSK1016790A application times. Furthermore, in recent control experiments we could not reproduce the finding shown in Fig. 3e + f that pre-incubating oocytes with BAPTA-AM reliably abolished the activation of endogenous calcium-activated chloride channels. We also realized that heterologous expression of human PAR_2 in oocytes was highly variable and functionally difficult to distinguish from the endogenous *Xenopus laevis* PAR_2-like receptor.

As it stands, the data shown in Figs. 4 to 9 do not allow any valid conclusion regarding PAR2-mediated TRPV4 sensitization by trypsin or by neutrophil elastase. In particular, we have no proof that Rho-kinase inhibitor Y27362 inhibits PAR2-mediated sensitization of TRPV4 by neutrophil elastase. Moreover, we cannot claim that PAR2-mediated TRPV4 sensitization is independent of intracellular calcium.

In contrast, the findings shown in Figs. 1 and 2 remain valid and demonstrate that the *Xenopus laevis* oocyte

The online version of the original article can be found at http://dx.doi.org/10.1007/s00424-014-1539-6

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expression system is useful to study human TRPV4 currents at the whole-cell and single channel level. Moreover, using a modified experimental protocol (unpublished data) we recently were able to demonstrate that activation of endogenous PAR2-like receptor by trypsin causes sensitization of human TRPV4 heterologously expressed in the oocyte system. This confirms the potential usefulness of this experimental system for future studies to elucidate the molecular mechanisms involved in PAR2-mediated TRPV4 sensitization.

We sincerely apologize for these regrettable errors and shortcomings in our manuscript and for any confusion that we may have caused to the readers of *Pflügers Archiv*.